FETAL ASCITES AND SECOND TRIMESTER MATERNAL HEPATITIS C VIRUS INFECTION

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SUMMARY

Objective: To present the first reported case of early second trimester maternal hepatitis C virus (HCV) associated with fetal ascites, which was treated with fetal paracentesis, and resulted in a successful outcome of a term liveborn infant with anti-HCV seropositivity.

Case Report: A 26-year-old primigravida woman was diagnosed with acute HCV infection at 17 weeks of gestation. Ultrasound (US) at 23 weeks showed significant fetal ascites and echogenic bowel, and fetal viral infection was suspected. Maternal serum was positive for high HCV-RNA titers and cytomegalovirus (CMV) IgG. Amniocentesis, cordocentesis and therapeutic fetal paracentesis were performed at 23 weeks. Fetal karyotype was 46,XX. Cord blood showed anti-HCV positivity and HCV-RNA titer < 10. Amniotic fluid was anti-HCV and CMV IgG positive. US at 27 weeks showed complete resolution of fetal ascites. A healthy 2,976 g female baby was delivered at 37 weeks, with anti-HCV seropositivity, high HCV-RNA titers, CMV IgG positive, IgM negative and normal liver function tests at the 1-month follow-up.

Conclusion: Second trimester perinatal HCV infection with possible CMV coinfection associated with fetal ascites is a rare event. Fetal therapy resulting in a successful outcome has not been reported. Prompt fetal therapy with paracentesis in this case led to the delivery of a healthy term liveborn baby with anti-HCV seropositivity.

Key Words: cytomegalovirus, fetal ascites, hepatitis C, paracentesis, prenatal diagnosis

Introduction

Hepatitis C virus (HCV) in pregnancy is relatively uncommon, with most studies reporting a prevalence of < 5% [1–3]. Reports of fetal complications in mothers infected with HCV are also limited and the risk of mother-to-infant transmission varies widely. Second trimester perinatal HCV infection with possible cytomegalovirus (CMV) coinfection that is associated with fetal ascites is a rare event; fetal therapy resulting in a successful outcome has not been reported. We report a case of early second trimester maternal HCV infection associated with fetal ascites, which was treated with fetal paracentesis, resulting in a term liveborn infant with anti-HCV seropositivity. Perinatal transmission and perinatal outcome associated with HCV and CMV infections are also discussed.

Case Report

A 26-year-old, gravida 1, para 0, woman with no history of hepatitis, blood transfusions or significant past medical or surgical history presented for prenatal care starting in the first trimester. Her gynecologic history was significant for a total of three past sexual partners, the last one being her current husband. She complained of anorexia and malaise of 1-week duration.
at 17 weeks’ gestation. She was found to have jaundice and had elevated liver function tests (LFTs) (aspartate aminotransferase, 333 IU; alanine aminotransferase, 753 IU) with total bilirubin of 4.9 mg/mL. At that time, she reported that her husband was anti-HCV seropositive due to blood transfusion after an operation during infancy. Hepatitis tests showed positive anti-HCV antibodies but were negative for hepatitis A and B. She declined testing for human immunodeficiency virus. She was asymptomatic by 21 weeks’ gestation.

Ultrasound (US) at 21 weeks showed an appropriate for gestational age sized 519 g female fetus with ascites but normal amniotic fluid volume (AFV). Level II US at 23 weeks showed a 717 g fetus with normal AFV, significant fetal ascites and fetal echogenic bowel, with an umbilical artery systolic/diastolic ratio of 3:1 (Figures 1 and 2). Fetal viral infection was suspected due to the maternal history of acute HCV infection during pregnancy. The option of termination of pregnancy was discussed and possible adverse fetal outcomes were reviewed with the patient; she decided to continue with the pregnancy. Amniocentesis, cordocentesis and therapeutic fetal paracentesis were performed at 23 weeks. Fetal karyotype was 46,XX. Amniotic fluid was positive for anti-HCV antibodies and CMV IgG but negative for CMV IgM and toxoplasmosis IgG and IgM. Fetal paracentesis was performed due to concern that pulmonary hypoplasia could develop from the marked upward displacement of the diaphragm. It was performed using a 22-gauge spinal needle with aspiration of 50 mL of straw-colored ascitic fluid. Fetal ascitic fluid was positive for anti-HCV antibody and CMV IgG (90.6 Au/mL) but not CMV IgM. The ascitic fluid was not evaluated for cell counts or biochemistry. The limited amount of cord blood obtained was positive for anti-HCV antibodies with an HCV-RNA titer < 10. The maternal serum HCV-RNA titer on the same day was 1,330,000 copies/mL (HCV-RNA type 1b) and positive for CMV IgG (250 Au/mL) but not IgM.

Follow-up US at 25 weeks showed minimal ascites, with complete resolution of fetal ascites by 27 weeks’ gestation. However, minimal fetal echogenic bowel was still present. Between 28 and 34 weeks, maternal LFTs were between 100 and 300 IU. The maternal HCV-RNA titer increased to 9,410,000 copies/mL at 34 weeks of gestation. US at this time showed a normal size 2,243 g fetus with normal AFV. There was no evidence of fetal ascites or other major fetal structural anomalies.

The patient delivered at 37 weeks by cesarean section due to fetal malpresentation following spontaneous rupture of membranes and labor. A 2,976 g female baby was delivered, with Apgar score of 9/10. At the 1-month neonatal visit, the infant had hemoglobin of 9.9 mg/mL, was CMV IgG positive (239 Au/mL) but IgM negative, had normal LFTs and was anti-HCV seropositive with a very high HCV-RNA titer of 17,883,600 copies/mL. The infant appeared to be healthy and had a normal physical examination. Maternal follow-up at 2.5 months postpartum showed an HCV-RNA titer of 557,078 copies/mL. Her husband was tested and was found to be carrying the same type of HCV-RNA (type 1b). Both the patient and infant were scheduled to return for follow-up examinations and laboratory tests at 6 months after delivery.

**Discussion**

Hepatitis C is a single-stranded RNA virus of the Flaviviridae family that is transmitted via infected blood or blood products, or sexually transmitted via saliva, vaginal secretions or semen. Although more...
prevalent in intravenous drug users, hemophiliacs and those with high-risk sexual behavior, only half of anti-HCV-positive persons have risk factors [1]. This patient likely contracted HCV from her husband during pregnancy as they both carry the same type of HCV-RNA and she has no other known risk factors or past history of hepatitis.

HCV in pregnancy is relatively uncommon, with most studies reporting a prevalence < 5% [2,3]. The prevalence of HCV in pregnancy in Taiwan is unknown as there is no routine screening for it during prenatal care. Antiviral treatment for HCV is usually not given during pregnancy. Currently, there are no known methods for the prevention of HCV transmission at birth. Perinatal transmission can occur while the fetus is in utero or during the intrapartum period, with an estimated reported rate of 0% to as high as 18% [4–7], and an average reported rate of approximately 5% [8–10]. Dunn et al [11] reported on the uncertainty associated with the diagnosis of HCV in children born to HCV-infected mothers, which is currently based on serologic assays and HCV-RNA measurement by polymerase chain reaction (PCR), due to lack of data about the age distribution of loss of maternal antibodies and specificity of PCR at different ages. Currently available data suggest that the presence of HCV-RNA in the neonate confirms vertical transmission of HCV and that passively transmitted maternal anti-HCV antibodies are detected in most of the neonates, persisting for 6–18 months [12,13]. Increased rates of vertical transmission have been noted in women with high HCV-RNA titers or concurrent HIV infection [5], drug use, viral genotype and vaginal deliveries [10]. This patient was viremic throughout the latter half of her pregnancy, with very high titers of HCV-RNA, thus increasing the chance of HCV transmission or infection of her fetus. Furthermore, the infant had a remarkably high HCV-RNA titer of 17,883,600 copies/mL at her 1-month neonatal follow-up visit.

We did not test for either maternal or fetal/neonatal HCV IgM in this case. This is because, although there are different diagnostic techniques for detecting HCV, the detection of specific IgG against HCV by means of enzyme immunoassays is the most practical method for diagnosing infection by this virus [14]. HCV-RNA detection using PCR can also be used for the diagnosis of HCV. The finding of HCV-RNA titer < 10 in antepartum fetal cord blood implies that there may not be active replication of HCV at the time when the sample was obtained. However, data suggest that mother-to-infant transmission of HCV is possible only in the case of HCV-RNA positive mothers [15], as in this case. Furthermore, the transmission of HCV from mother to infant appears to correlate with the level of maternal circulating viral load [16]. Given the presence of both anti-HCV antibodies, high maternal and later neonatal HCV-RNA viral loads, and the same HCV type Ib genotype, vertical transmission of HCV can be confirmed in this case.

We postulate that the fetus acquired HCV in utero given the timing and severity of the second trimester maternal acute HCV infection, high HCV-RNA levels and coincidental finding of fetal ascites. Rupture of the amniotic membrane may have exposed the fetus to further HCV viral loads.

This patient’s case was further complicated by the question of concomitant CMV infection, with positive CMV IgG but negative CMV IgM noted during her pregnancy. The presence of CMV IgG in the fetus/infant and maternal blood has been reported to be of limited value given the high prevalence of CMV IgG in women of childbearing age, and preexisting maternal CMV immunity has been reported to strongly reduce perinatal transmission [16]. Clinically apparent sequelae from congenital CMV infections are less often associated with recurrent maternal infection reactivation than with primary infections. As both maternal and fetal CMV IgM were negative in this case, we do not highly suspect congenital CMV coinfection, although we cannot definitively rule it out. Congenital fetal chylous ascites was not suspected as it has been reported to be usually associated with polyhydramnios [17], which was not present in this case. We believe that HCV played a major role in the fetal ascites in this case, given the timing of maternal acute clinical hepatitis infection, maternal high viral load and subsequent sonographic findings of fetal ascites. The fact that the maternal serum, fetal ascitic fluid and infant’s blood all tested negative for CMV IgM antibodies, in conjunction with similar levels of CMV IgG being found in both maternal and infant sera, made passive transplacental transfer of CMV IgG a more likely possibility. Longer follow-up of the infant, along with serial serologic testing for CMV and HCV antibodies and HCV-RNA levels are required to clarify this issue.

In conclusion, second trimester maternal HCV infection associated with fetal ascites is a rare event; fetal therapy in the second trimester resulting in a successful outcome has not been reported. This patient had acute HCV infection in the second trimester and subsequently developed fetal ascites. The high neonatal HCV viral load points to HCV playing a possible major role in the neonate’s condition. Prompt fetal therapy with paracentesis contributed to early resolution of the fetal ascites, resulting in the delivery of a term liveborn infant with normal Apgar scores and anti-HCV seropositivity.
References


